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AB Repulsive guidance molecule (RGM) is a recently identified protein implicated in both axonal guidance and neural tube closure. The avoidance of chick RGM in the posterior optic tectum by growing temporal, but not nasal, retinal ganglion cell axons is thought to contribute to visual map formation. In contrast to ephrins, semaphorins, netrins and slits, no receptor mechanism for RGM action has been defined. Here, an expression cloning strategy identified neogenin as a binding site for RGM, with a sub-nanomolar affinity. Consistent with selective axonal responsiveness to RGM, neogenin is expressed in a gradient across the chick retina. Neogenin is known to be one of several netrin-binding proteins but only neogenin interacts with RGM. The avoidance of RGM by temporal retinal axons is blocked by the anti-neogenin antibody and the soluble neogenin ectodomain. Dorsal root ganglion axons are unresponsive to RGM but are converted to a responsive state by neogenin expression. Thus, neogenin functions as an RGM receptor.

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